eurofins | BioPharma Product Testing

in cooperation with BIOSERVICE SCIENTIFIC LABORATORIES

Acute Dermal Irritation/Corrosion in the Rabbit with [redacted]

Report

Version: Final

Eurofins Munich / BSL Munich Study No.: [redacted]

Sponsor:

[redacted]

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1. Copies of the GLP Certificates

Bayerisches Landesamt für
Gesundheit und Lebensmittelsicherheit

GLP-Bescheinigung/Statement of GLP Compliance
(gemäß/according to § 19b Abs. 1 Chemikaliengesetz)

Eine GLP-Inspektion zur Überwachung der Einhaltung der GLP-Grundsätze gemäß Chemikaliengesetz bzw. Richtlinie 2004/9/EG wurde durchgeführt in:

Assessment of conformity with GLP according to Chemikaliengesetz and Directive 2004/9/EC at:

☒ Prüfeinrichtung/Test facility ☐ Prüfstandort/Test site

EUROFINS BIOPHARMA PRODUCT TESTING MUNICH GMBH
BEHRINGSTRAßE 6-8
82152 PLANEGG

(Unverwechselbare Bezeichnung und Adresse/Unequivocal name and address)

Prüfungen nach Kategorien/Areas of Expertise
(gemäß/according ChemVwV-GLP Nr. 5.3/OECD guidance)

Kategorie 2/ Category 2
Kategorie 3/ Category 3
Kategorie 8/ Category 8
Kategorie 9*/ Category 9*

*Sonstige Prüfungen:	*other tests:
biologische und mikrobiologische Sicherheitsprüfungen an Medizinprodukten und Arzneimitteln; Auftragsarchivierung	*biological an microbiological safety evaluation on medical devices and pharmaceuticals; contract archiving*

Datum der Inspektion/Date of Inspection
(Tag.Monat.Jahr/day.month.year)

18. bis 19.03.2015

Die/Der genannte Prüfeinrichtung/Prüfstandort befindet sich im nationalen GLP-Überwachungsverfahren und wird regelmäßig auf Einhaltung der GLP-Grundsätze überwacht.

The above mentioned test facility/test site is included in the national GLP Compliance Programme and is inspected on a regular basis.

Auf der Grundlage des Inspektionsberichtes wird hiermit bestätigt, dass in dieser Prüfeinrichtung/ diesem Prüfstandort die oben genannten Prüfungen unter Einhaltung der GLP-Grundsätze durchgeführt werden können.

Based on the inspection report it can be confirmed, that this test facility/test site is able to conduct the aforementioned studies in compliance with the Principles of GLP.

Schwabach, 05.06.2015 [redacted]

GLP- Landesleitstelle Bayern
Bayerisches Landesamt für Gesundheit
und Lebensmittelsicherheit
Rathausgasse 4
91126 Schwabach

Bayerisches Landesamt für
Gesundheit und Lebensmittelsicherheit

GLP-Bescheinigung/Statement of GLP Compliance
(gemäß/according to § 19b Abs. 1 Chemikaliengesetz)

Eine GLP-Inspektion zur Überwachung der Einhaltung der GLP-Grundsätze gemäß Chemikaliengesetz bzw. Richtlinie 2004/9/EG wurde durchgeführt in:

Assessment of conformity with GLP according to Chemikaliengesetz and Directive 2004/9/EC at:

☒ Prüfeinrichtung/Test facility ☐ Prüfstandort/Test site

BSL BIOSERVICE
SCIENTIFIC LABORATORIES MUNICH GMBH
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82152 PLANEGG
(Unverwechselbare Bezeichnung und Adresse/Unequivocal name and address)

Prüfungen nach Kategorien/Areas of Expertise
(gemäß/according ChemVwV-GLP Nr. 5.3/OECD guidance)
Kategorie 2/Category 2
Kategorie 9*/ Category 9*

*Sonstige Prüfungen:	*other tests:
Bioaktivitätsprüfungen	*Bioactivity testing*

Datum der Inspektion/Date of Inspection
(Tag.Monat.Jahr/day.month.year)

18. bis 19.03.2015

Die/Der genannte Prüfeinrichtung/Prüfstandort befindet sich im nationalen GLP-Überwachungsverfahren und wird regelmäßig auf Einhaltung der GLP-Grundsätze überwacht.

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[redacted]

Schwabach, 05.06.2015

GLP- Landesleitstelle Bayern
Bayerisches Landesamt für Gesundheit
und Lebensmittelsicherheit
Rathausgasse 4
91126 Schwabach

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4. Preface

4.1. Abbreviations

AAALAC	Association for Assessment and Accreditation of Laboratory Animal Care
ABS	acrylonitrile butadiene styrene
BGBl.	Bundesgesetzblatt *(Federal Law Gazette)*
BSL Munich	BSL BIOSERVICE Scientific Laboratories Munich GmbH
EC	European Commission
EEC	European Economic Community
e.g.	exempli gratia (for example)
EPA	Environmental Protection Agency
Eurofins Munich	Eurofins BioPharma Product Testing Munich GmbH
GHS	Globally Harmonised System of Classification and Labelling of Chemicals
GLP	Good Laboratory Practice
GmbH	Gesellschaft mit beschränkter Haftung *(company with limited liability)*
GV-SOLAS	Gesellschaft für Versuchstierkunde *(Society for Laboratory Animal Science)*
NZW	New Zealand White
OECD	Organisation for Economic Cooperation and Development
OPPTS	Office of Prevention, Pesticides and Toxic Substances
QAU	Quality Assurance Unit
SOPs	Standard Operating Procedures
SPF	specific-pathogen free
TVT	Tierärztliche Vereinigung für Tierschutz *(Veterinary Association for Animal Welfare)*

4.2. General

Sponsor:	[redacted]
Study Monitor:	[redacted]
Test Facility:	BSL BIOSERVICE Scientific Laboratories Munich GmbH Behringstr. 6/8 82152 Planegg Germany
Eurofins Munich / BSL Munich Study No.:	[redacted]
Test Item:	[redacted]
Title:	Acute Dermal Irritation/Corrosion in the Rabbit with [redacted]

4.3. Project Staff

Study Director:	[redacted] BSL BIOSERVICE Scientific Laboratories Munich GmbH Behringstr. 6/8 82152 Planegg Germany
Head of GLP Quality Assurance Unit:	[redacted] Eurofins BioPharma Product Testing Munich GmbH Behringstr. 6/8 82152 Planegg Germany

4.4. Schedule

Arrival of the Test Item:	11 November 2016
Study Initiation Date:	16 February 2017
Experimental Starting Date:	19 February 2017
Experimental Completion Date:	03 March 2017
Study Completion Date:	date of the study director's signature

5. Quality Assurance

5.1. GLP Compliance

This study was conducted to comply with:

Chemikaliengesetz ("Chemicals Act") of the Federal Republic of Germany, Appendix 1 to § 19a as amended and promulgated on August 28, 2013 (BGBl. I S. 3498) [1].

Konsens-Dokument der Bund-Länder-Arbeitsgruppe Gute Laborpraxis ("Consensus Document of the National and Länder Working Party on Good Laboratory Practice") on the archiving and storage of records and materials, 5 May 1998 [2].

OECD Principles of Good Laboratory Practice (as revised in 1997); OECD Environmental Health and Safety Publications; Series on Principles of Good Laboratory Practice and Compliance Monitoring - Number 1. Environment Directorate, Organisation for Economic Co-operation and Development, Paris 1998 [3].

The OECD Principles of Good Laboratory Practice are accepted by regulatory authorities throughout the European Community, USA and Japan.

This study was assessed for compliance with the study plan and the Standard Operating Procedures of Eurofins Munich and BSL Munich. The study and/or the test facility are inspected periodically by the Quality Assurance Unit according to the corresponding SOPs. These inspections and audits are carried out by the Quality Assurance Unit of Eurofins Munich which was independent of the staff involved in the study. A signed quality assurance statement, listing all performed audits, is included in the report.

5.2. Guidelines

This study followed the procedures indicated by internal Eurofins Munich and BSL Munich SOPs and the following internationally accepted guidelines and recommendations:

OECD Guidelines for Testing of Chemicals, No. 404, "Acute Dermal Irritation/Corrosion" adopted 28 July 2015 [4]

Commission Regulation (EC) No 440/2008, L 142, Annex Part B, Method B.4, 30 May 2008 [5]

EPA Health Effects Test Guidelines, OPPTS 870.2500 "Acute dermal irritation", EPA 712-C-98-196, (August 1998) [6]

Procedures and facilities comply with the requirements of Directive 2010/63/EU [7] and the national legislation defined in the animal protection law concerning the protection of animals used for experimental and other scientific procedures [8].

5.3. Archiving

For a period of 15 years (or shorter if in compliance with the GLP regulations) Eurofins Munich will store the records, materials and specimens in their scientific archives according to the GLP regulations.

The following records have to be stored according to the GLP regulations:

A copy of the final report, the study plan and a documentation of all raw data generated during the conduct of the study (documentation forms as well as any other notes of raw data, printouts of instruments and computers) and the correspondence with the sponsor concerning the study. Any document relating to the study will be discarded only with the prior consent of the sponsor.

The following materials and samples have to be stored according to the period of time specified in the GLP regulations:

A retained sample of the test item will be archived according to the GLP regulations, if possible, and will be discarded without the sponsor's prior consent.

Other materials and specimens have to be stored according to the GLP regulations and disposed of after the respective archiving period with the sponsor's prior consent.

As requested, only new unneeded test item will be returned to the sponsor.

6. Statement of Compliance

Eurofins Munich / BSL Munich Study No.: [redacted]

Test Item: [redacted]

Title: Acute Dermal Irritation/Corrosion in the Rabbit with [redacted]

Study Director: [redacted]

This study performed in the test facility BSL Munich was conducted in compliance with Good Laboratory Practice Regulations:

Chemikaliengesetz ("Chemicals Act") of the Federal Republic of Germany, Appendix 1 to § 19a as amended and promulgated on August 28, 2013 (BGBl. I S. 3498) [1].

Konsens-Dokument der Bund-Länder-Arbeitsgruppe Gute Laborpraxis ("Consensus Document of the National and Länder Working Party on Good Laboratory Practice") on the archiving and storage of records and materials, 5 May 1998 [2].

"OECD Principles of Good Laboratory Practice (as revised in 1997)", Paris 1998 [3].

There were no circumstances that may have affected the quality or integrity of the study.

Study Director: [redacted]

Date: 24 Apr 2017

7. Statement of the Quality Assurance Unit

Eurofins Munich / BSL Munich
Study No.: [redacted]

Test Item: [redacted]

Title: [redacted]

Study Director: [redacted]

This report and the conduct of this study were inspected by the Quality Assurance Unit (Eurofins Munich) on the following dates:

Phase of QAU Inspection	Date of QAU Inspection	Date of Reporting to the Study Director and Management
Audit Final Study Plan:	16 February 2017	16 February 2017
Audit Experimental Phase (process-based):	25 January 2017	25 January 2017
Audit Final Report:	20 APR 2017	20 APR 2017

This report reflects the raw data.

Member of the
Quality Assurance Unit:

..... [redacted] .....
Prin

Date: 25 APR 2017 .....

8. Summary

8.1. Summary Results

On the basis of the test results given below and in conformity with the criteria given in Annex I of Regulation (EC) 1272/2008 [9], the substance should be:

classified into category 1	☐
classified into category 2	☐
not classified	☒

On the basis of the test results given below and in conformity with the criteria given in GHS (Globally Harmonized System of Classification and Labelling of Chemicals) [10], the substance should be:

classified into category 1	☐
classified into category 2	☐
classified into category 3	☐
not classified	☒

Species/strain:	New Zealand White Rabbits Crl: KBL (NZW)
Number of animals:	2
Duration of exposure:	4 hours
Amount of substance:	0.5 g per test site
Type of dressing:	semi-occlusive
Vehicle (moistening):	aqua ad injectionem
First time of effects:	no effects observed
Last time of effects:	no effects observed
Reversibility of the observed effects:	no effects observed
Method:	OECD 404 [4] EC 440/2008, Method B.4 [5] OPPTS 870.2500 [6]

Table 1: Average Irritation Scores – (24, 48, 72-hour reading) – and Total Mean Value

Mean Value Irritation Scores		
Animal No.	**Mean 24 – 72 hours**	
	Erythema	**Oedema**
1	0	0
2	0	0
Total Mean Value	**0**	**0**

8.2. Conclusion

Under the conditions of the present study, the single dermal application of the test item [redacted] to two rabbits at a dose of 0.5 g showed neither irritant nor corrosive effects.

Neither mortalities nor significant clinical signs of toxicity were observed.

According to Annex I of Regulation (EC) 1272/2008 [9], the test item [redacted] does not have to be classified and has no obligatory labelling requirement for skin irritation.

According to GHS (Globally Harmonized Classification System) [10], the test item [redacted] has no obligatory labelling requirement for skin irritation.

For details of the classification criteria see chapter 16.

9. Introduction

9.1. Justification for the Selection of the Test System

The test for acute dermal irritation/corrosion is performed on the rabbit.

Prior to initiation of the test, the test item was assessed not to fulfill one of the following criteria which would preclude testing:

a) materials that have predictable corrosive potential based on structure-activity relationships and/or physicochemical properties such as strong acidity or alkalinity, e.g., when the material to be applied has a pH of 2 or less or 11.5 or greater

b) materials which have been proved to be highly toxic by the dermal route

c) materials which, in an acute dermal toxicity test, have been shown to produce irritation of the skin at the limit test dose level of 2000 mg/kg body weight

d) materials which have been proved to be corrosive by the in-vitro skin corrosion test

9.2. Justification for the Selection of the Test Method

An *in-vitro* skin irritation (Human Skin Model Test, OECD guideline number 439) was performed with [redacted] (Eurofins Munich Study No. 168402). Given the fact that the test substance was incompatible with the in vitro test system, the in-vivo test was performed.

10. Materials and Methods

10.1. Characterisation of the Test Item

The identity of the test item was inspected upon delivery at the test facility (e.g. test item name, batch no. and additional data were compared with the label) based on the following specifications provided by the sponsor.

Name:	[redacted]
Common Name:	[redacted]
Batch No.:	Exp.127
Physical State:	powder
Colour:	brownish red
Storage Conditions:	room temperature
Safety Precautions:	The routine hygienic procedures were sufficient to assure personnel health and safety.

10.2. Preparation of the Test Item

The test item was used as delivered by the sponsor.

In order to ensure good skin contact, it was moistened with aqua ad injectionem (AlleMan Pharma, lot no. 601101, expiry date: 12/2018)

The vehicle was chosen due to its non-irritating characteristics.

10.3. Weight-of-Evidence Analysis

In order to avoid the unnecessary use of animals and to minimise any testing that is likely to produce severe responses in animals, a weight-of-evidence analysis was performed with the available data (data from the test substance data sheet). The paperwork is archived in the project file. Additionally the confirmation in writing that the studies are required for submission to regulatory authorities or to fulfil obligations postulated by law was taken into account.

10.4. Test System

Species/strain:	healthy New Zealand White Rabbits, Crl: KBL (NZW)
Source:	Charles River Deutschland, 97633 Sulzfeld, Germany
Sex:	male
Body weight at the beginning of the study:	> 2 kg
Age at the beginning of the study:	animal no. 1: approximately 51 weeks old animal no. 2: approximately 53 weeks old
Number of animals:	2

The animals were derived from a controlled full-barrier maintained breeding system (SPF). According to the German Act on Animal Welfare [8] the animals were bred for experimental purposes.

This study was performed in an AAALAC-accredited laboratory. According to German animal protection law, the study type has been reviewed and accepted by local authorities. Furthermore, the

study has been subjected to Ethical Review Process and was authorised by the Bavarian animal welfare administration.

10.4.1. Housing and Feeding Conditions

- Semi barrier in an air-conditioned room
- Temperature: 18 ± 3 °C (recommendations of TVT [11], GV-SOLAS [12])
- Relative humidity: 55 ± 10%
- Artificial light, sequence being 12 hours light, 12 hours dark
- Air change: at least 10 x / hour
- Free access to autoclaved hay and to Altromin 2123 maintenance diet for rabbits, rich in crude fibre
- Free access to tap water (drinking water, municipal residue control, microbiological controls at regular intervals)
- Certificates of food, water and bedding are filed for two years at BSL Munich and afterwards archived at Eurofins Munich
- Housed in ABS-plastic or Noryl rabbit cages, floor 4200 cm^2
- Adequate acclimatisation period (at least 5 days) under laboratory conditions

10.5. Preparation of the Animals

Approximately 24 hours before the test, the fur was removed from the dorsal area of the trunk by using an electric clipper. Care was taken to avoid abrading the skin, and only animals with healthy intact skin were used.

10.6. Initial Test (In Vivo Dermal Irritation/Corrosion Test Using One Animal)

The test item was not expected to produce corrosion, but might be irritating. Therefore, a single patch was applied to one animal for 4 hours.

10.7. Application

The test item was applied at a single dose to a small area (approximately 6 cm^2) of skin on one side of the dorsal area and covered with a gauze patch, which was held in place with a non-irritating tape. The untreated other side served as control. The test item was applied to the patch first and then applied to the skin. To ensure good skin contact, the test item was moistened with the vehicle. The patch was fixed with a semi-occlusive dressing. The limits of the application site were marked with an ink marker.

10.8. Dose Level

A dose of 0.5 g of the test item was applied to each test site.

10.9. Exposure Period

The test item was held in contact with the skin throughout a 4-hour period.

At the end of the exposure period, the residual test item was removed with [redacted] which was chosen as best solvent for this purpose after testing physiological saline 0.9% NaCl, 70% ethanol, dimethylsulfoxid, corn oil and acetone.

10.10. Confirmatory Test

The results of the initial test did not indicate the test item to be corrosive or a severe irritant to the skin using the procedure described. In order to confirm the response, one additional animal was treated in the same manner. According to OECD 404, section 17, treatment of a third animal can be omitted when animal no. 1 and 2 exhibit the same response. Also, considering the classification directives (see chapter 16) the results of animal no. 1 and 2 were sufficient for classification of the test item. Moreover, as the test item showed no signs of corrosion in two animals, it is considered that adding a third animal would not change the outcome of the study.

10.11. Observation Period

The animals were observed for 72 hours after the patch removal.

10.12. Clinical Observation

The animals were examined for signs of erythema and oedema 1 hour after the patch removal. For the determination of classification-relevant values, the animals were examined for signs of erythema and oedema 24, 48 and 72 hours after the patch removal. Dermal irritation was scored and recorded according to the grades in the table below (Table 2). Any other signs such as hyperplasia, scaling, discolouration, fissures and scabs or any systemic effects were also recorded.

For the initial test in one animal, the test site was also examined immediately after the patch had been removed.

Table 2: Scoring System

Erythema and Eschar Formation	**Score**
No erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate to severe erythema	3
Severe erythema (beef redness) to eschar formation preventing grading of erythema	4
Oedema Formation	**Score**
No oedema	0
Very slight oedema (barely perceptible)	1
Slight oedema (edges of area well defined by definite raising)	2
Moderate oedema (raised approximately 1 mm)	3
Severe oedema (raised more than 1 mm and extending beyond exposure area)	4

10.13. Body Weight

The animals were weighed prior to the administration and at the end of the observation period.

10.14. Evaluation of Results

Individual reactions for each animal were recorded according to the scoring system described in Table 2 at each time of observation.

Nature, severity and duration of clinical observations were described.

The body weight changes were summarised in a tabular form.

For details of the classification criteria see chapter 16.

11. Deviations from the Study Plan

There were no deviations from the study plan.

12. Results

Neither irritant nor corrosive effects were observed on the intact skin of two male rabbits (strain NZW) after a contact time of 4 hours (Table 3 - Table 4).

Evaluation of the test item application site was partly impaired by discolouration of the skin due to residual test item.

Neither mortalities nor significant clinical signs of toxicity were observed.

The individual values for each animal were recorded according to the scoring system described in 10.12 (see Table 2).

Table 3: Individual Data - Evaluation of Dermal Irritation

Animals No.	Timepoint	Irritation					
		Oedema		Erythema		Comment	
		Test Item	Control	Test Item	Control	Test Item	Control
1	0h	0	0	0*	0	-	-
	1h	0	0	0*	0	-	-
	24h	0	0	0*	0	-	-
	48h	0	0	0*	0	-	-
	72h	0	0	0*	0	-	-
2	1h	0	0	0*	0	-	-
	24h	0	0	0*	0	-	-
	48h	0	0	0	0	-	-
	72h	0	0	0	0	-	-

0-4 = grade; * = evaluation partly impaired by discolouration due to residual test item

12.1. Clinical Observation

No adverse changes apart from the reactions in Table 3 were observed at the skin sites (see Table 4).

Table 4: Clinical Signs

Animals No.	Timepoint	Systemic Findings	Local Findings*		Comment	
		Test Item	Test Item	Control	Test Item	Control
1	0h	nsf	nsf	nsf	-	-
	1h	nsf	nsf	nsf	-	-
	24h	nsf	nsf	nsf	-	-
	48h	nsf	nsf	nsf	-	-
	72h	nsf	nsf	nsf	-	-
2	1h	nsf	nsf	nsf	-	-
	24h	nsf	nsf	nsf	-	-
	48h	nsf	nsf	nsf	-	-
	72h	nsf	nsf	nsf	-	-

* = apart from erythema/oedema; nsf = no specific findings

12.2. Body Weight Development

There were no significant body weight changes during the observation period (Table 5).

Table 5: Absolute Body Weights (kg)

Animal No.	Bodyweight (kg)	
	Start of Study	72 Hours Post Application
1	3.7	3.8
2	3.7	3.8

13. Conclusion

Under the conditions of the present study, the single dermal application of the test item [redacted] to two rabbits at a dose of 0.5 g showed neither irritant nor corrosive effects.

Neither mortalities nor significant clinical signs of toxicity were observed.

According to Annex I of Regulation (EC) 1272/2008 [9], the test item [redacted] does not have to be classified and has no obligatory labelling requirement for skin irritation.

According to GHS (Globally Harmonized Classification System) [10], the test item [redacted] has no obligatory labelling requirement for skin irritation.

For details of the classification criteria see chapter 16.

14. Distribution of the Report

1 original (paper):	Sponsor
1 copy (paper):	Eurofins Munich
1 copy (electronic):	Sponsor

15. References

15.1. Guidelines

[1] Chemikaliengesetz ("Chemicals Act") of the Federal Republic of Germany, Appendix 1 to § 19a as amended and promulgated on August 28, 2013 (BGBl. I S. 3498)

[2] Konsens-Dokument der Bund-Länder-Arbeitsgruppe Gute Laborpraxis ("Consensus Document of the National and Länder Working Party on Good Laboratory Practice") on the archiving and storage of records and materials, 5 May 1998

[3] OECD Principles of Good Laboratory Practice (as revised in 1997); OECD Environmental Health and Safety Publications; Series on Principles of Good Laboratory Practice and Compliance Monitoring - Number 1. Environment Directorate, Organisation for Economic Co-operation and Development, Paris 1998

[4] OECD Guidelines for Testing of Chemicals, Health Effects, No. 404, Acute Dermal Irritation/Corrosion (2015), Organisation for Economic Co-Operation and Development, Paris

[5] Commission Regulation (EC) No 440/2008, L 142, Annex Part B, Method B.4 of 30 May 2008 laying down test methods pursuant to Regulation (EC) No. 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)

[6] EPA Health Effects Test Guidelines, OPPTS 870.2500 Acute Dermal Irritation, EPA 712-C-98-196, August 1998, United States, Environmental Protection Agency, Prevention, Pesticides and Toxic Substances (7101)

[7] Directive 2010/63/EU of the European parliament of the council of 22 September 2010 on the protection of animals used for scientific purposes

[8] Deutsches Tierschutzgesetz (German Animal Welfare Act), 24. Juli 1972 (BGBl. I S. 1277)

[9] Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006. Official Journal of the European Communities, L 353, 31 December 2008

[10] GHS - Globally Harmonized System of Classification and Labelling of Chemicals. Sixth revised edition, United Nations. New York / Geneva, 2015.

[11] TVT Tierärztliche Vereinigung für Tierschutz, Merkblatt 127 zur Tiergerechten Haltung von Versuchskaninchen, 2010

[12] Planung, Struktur von Versuchstierbereichen tierexperimentell tätiger Institutionen; Veröffentlichung GV-SOLAS (Gesellschaft für Versuchstierkunde, Society for Laboratory Animal Science), Mai 1988

15.2. Internal Eurofins Munich and BSL Munich SOPs

Standard Operating Procedures (SOPs) No. 11-2-1

16. Appendix - Classification Criteria

On the basis of the test results, the test substance may be classified into one of the following categories in conformity with the criteria given in *Annex I of Regulation (EC) 1272/2008* [9]:

Category	Criteria	Hazard Communication Elements	
1 A, B, C	Destruction of skin tissue, with subcategorisation based on exposure of up to 3 minutes (A), 1 hour (B), or 4 hours (C)	Symbol:	Corrosion symbol
		Signal word:	Danger
		Hazard statement:	Causes severe skin burns and eye damage
2	Mean value of ≥ 2.3 ≤ 4.0 for erythema / eschar or edema in at least 2 of 3 tested animals from gradings at 24, 48, and 72 hours (or on 3 consecutive days after onset if reactions are delayed); inflammation that persists to the end of the (normally 14-day) observation period in at least 2 animals, particularly taking into account alopecia (limited area), hyperkeratosis, hyperplasia, and scaling; in some cases where there is pronounced variability of response among animals, with very definite positive effects related to chemical exposure in a single animal but less than the criteria above.	Symbol:	Exclamation mark
		Signal word:	Warning
		Hazard statement:	Causes skin irritation

On the basis of the test results, the test substance may be classified into one of the following categories in conformity with the criteria given in *GHS - Globally Harmonized System of Classification and Labelling of Chemicals, sixth revised edition, 2015* [10]:

Category	Criteria	Hazard Communication Elements	
1 A, B, C	Destruction of skin tissue, with subcategorisation based on exposure of up to 3 minutes (A), 1 hour (B), or 4 hours (C).	Symbol:	Corrosion symbol
		Signal word:	Danger
		Hazard statement:	Causes severe skin burns and eye damage
2	Mean value of ≥ 2.3 ≤ 4.0 for erythema / eschar or edema in at least 2 of 3 tested animals from gradings at 24, 48, and 72 hours (or on 3 consecutive days after onset if reactions are delayed); inflammation that persists to the end of the (normally 14-day) observation period in at least 2 animals, particularly taking into account alopecia (limited area), hyperkeratosis, hyperplasia, and scaling; in some cases where there is pronounced variability of response among animals, with very definite positive effects related to chemical exposure in a single animal but less than the criteria above.	Symbol:	Exclamation mark
		Signal word:	Warning
		Hazard statement:	Causes skin irritation
3	Mean value of ≥ 1.5 < 2.3 for erythema / eschar or oedema in at least 2 of 3 tested animals from gradings at 24, 48, and 72 hours (or on 3 consecutive days after onset if reactions are delayed).	Symbol:	No symbol
		Signal word:	Warning
		Hazard statement:	Causes mild skin irritation

No classification or labelling unless category 1-3 criteria are met.